



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANT(s): QIN, Yixian, et al. **EXAMINER:** BOR, Helene Catherine
SERIAL NO.: 10/522,452 **ART UNIT:** 3768
FILED: June 20, 2005 **DATE:** May 13, 2007
FOR: **METHOD AND APPARATUS FOR SCANNING CONFOCAL
ACOUSTIC DIAGNOSTIC FOR BONE QUALITY**

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

**37 C.F.R. § 1.131 DECLARATION OF PRIOR INVENTION
TO OVERCOME CITED ARTICLE**

I, Yixian Qin, submit this Declaration to establish reduction to practice of the invention of the above-referenced patent application prior to November 28, 2000, which is the filing date of Provisional Patent Application Serial Number 60/253,959, to which U.S. Patent No. 6,875,176 claims priority. U.S. Patent No. 6,875,176 was granted to Mourad et al. and was cited in an Office Action dated March 13, 2007, in regard to a rejection of the pending claims in the above-referenced patent application.

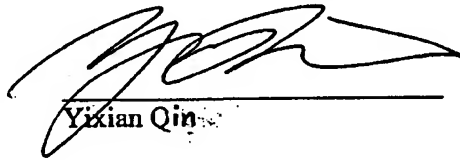
I hereby declare that:

1. I am an inventor of the above-referenced patent application.
2. Exhibits A and B attached hereto are submitted as evidence of a date of reduction to practice of the invention of the above-referenced patent application prior to November 28, 2000, which is the earliest priority date to which U.S. Patent No.

6,875,176 to Mourad et al. could claim priority, via Provisional Patent Application Serial Number 60/253,959.

3. Exhibit A is a nine (9) page presentation that I developed prior to November of 2000.
4. Exhibit B is a four (4) page publicity piece making reference to work being performed in regard to my invention.
5. I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of the United States Code, and that such willful false statement may jeopardize the validity of the application or any patent issuing thereon.

Date: June 1, 2007



Yixian Qin

A Scanning Confocal Acoustic Diagnostic for Bone Quality

Yvian Qin
Biomedical Engineering
State University of New York at Stony Brook

Supported by Innovative Technology Grant

Background

- Osteoporosis – A leading cause of bone fractures
- 25 million people suffer from osteoporosis in the US alone
- 1.3 million fractures are attributed to osteoporosis annually
- Annual direct cost over 15 billion US dollars
- 1/3 of women over 65 have vertebral fractures
- 90% of women over 75 have X-ray evidence of osteoporosis

Current noninvasive diagnostic methods

- Dual energy X-ray absorptiometry (DEXA)
- Single and dual photon absorptiometry (SPA & DPA)
- Computerized tomography (CT)
- All based on X-ray

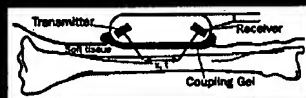
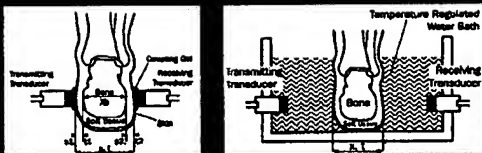
Current noninvasive diagnostic methods (cont.)

- DEXA is the best and most common tech in multi-sites, resolution and precision, but,
- Insensitive, certain bone must be lost before significance can be detected by DEXA
- Only provide an index with age risk
- Radiation and high cost (\$150k for machine alone)

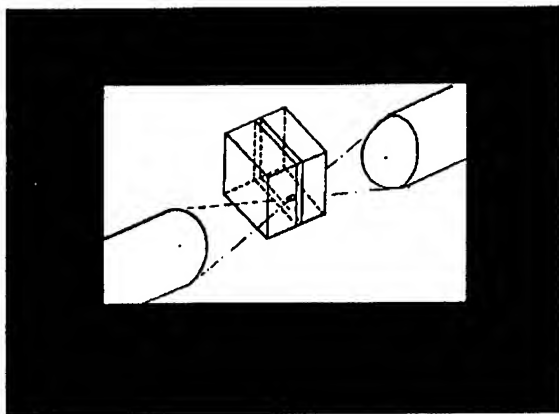
Ultrasonic Techniques

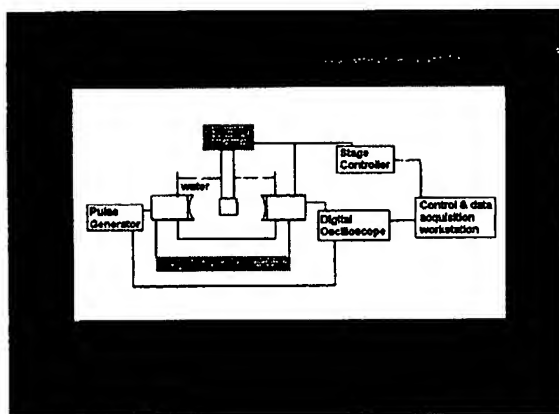
- Non-invasive
- Non-destructive
- Non-radiation
- Accurate

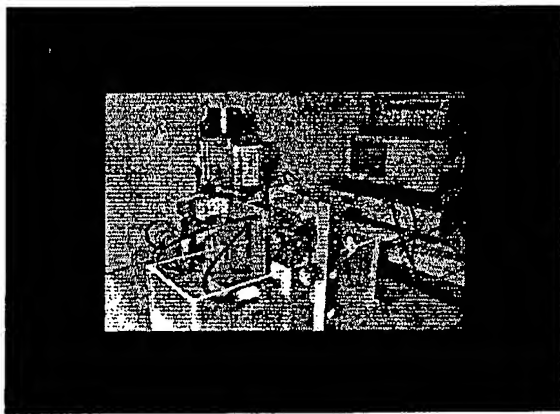
Ultrasonic techniques are used to measure bone density and bone quality. They are non-invasive and non-destructive, and do not involve radiation.

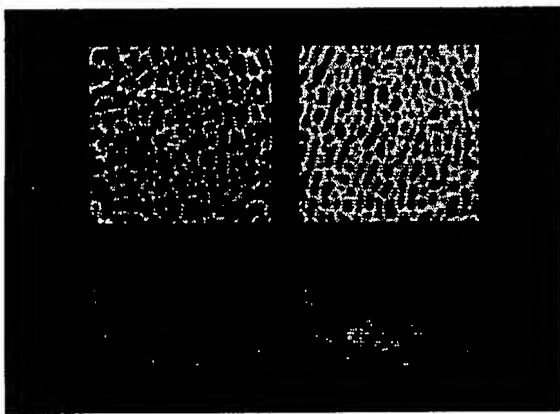


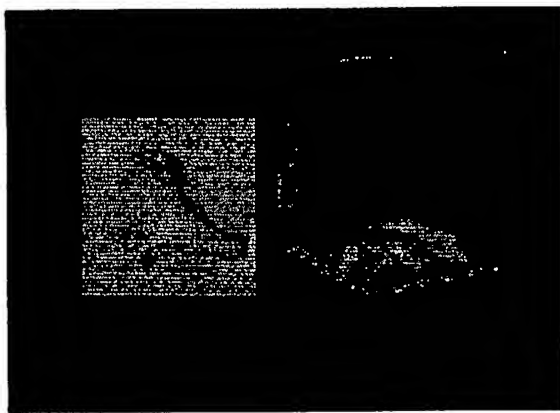


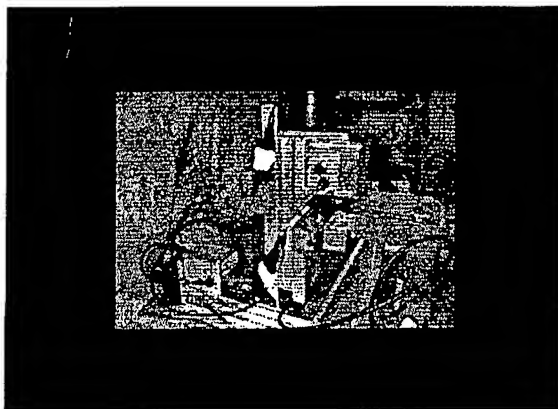


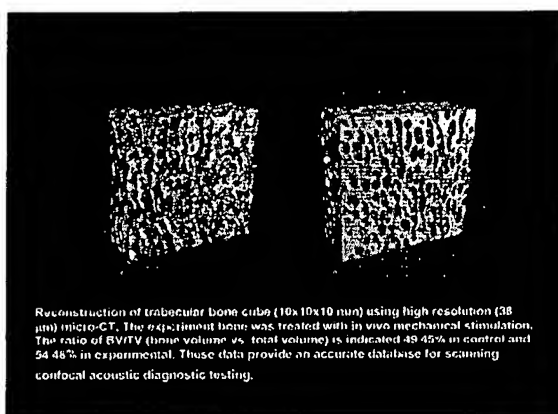


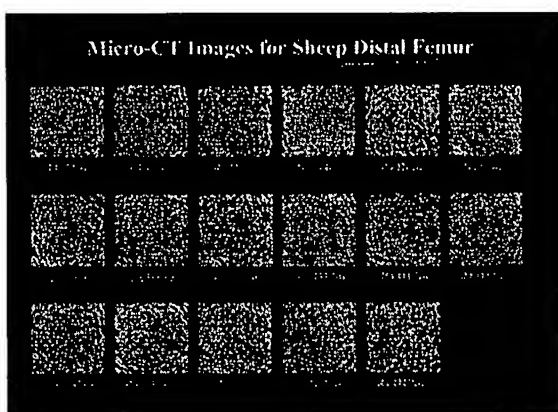


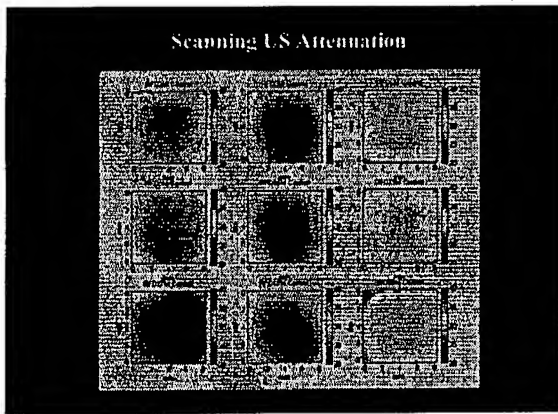


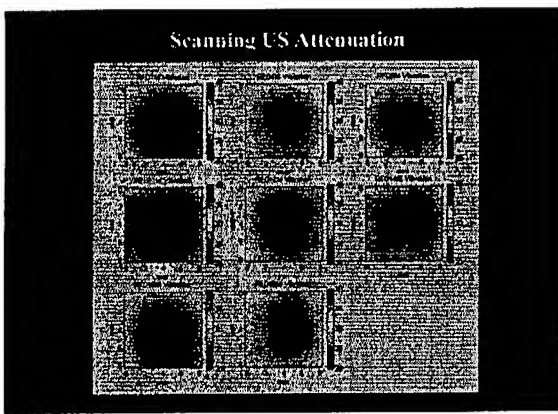


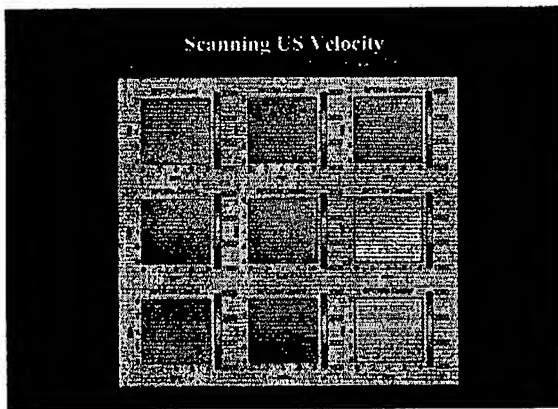


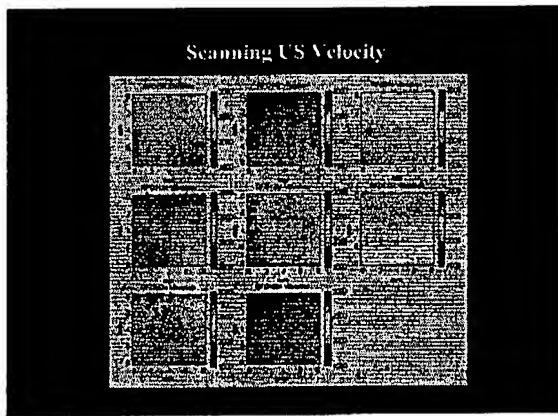


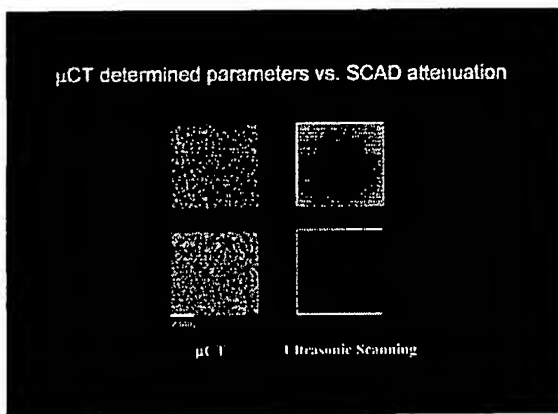


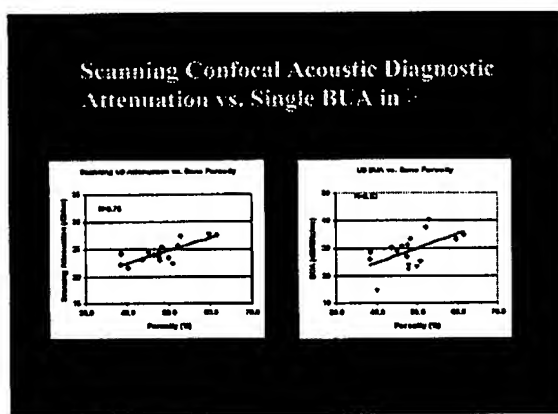




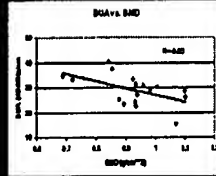
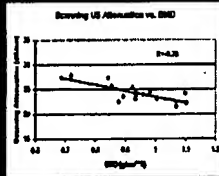




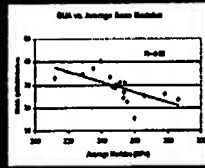
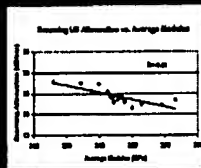




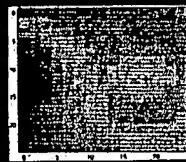
Scanning Confocal Acoustic Diagnostic Attenuation vs. Single BUA in $\text{cm}^2/\text{s}^2/\text{g}$



Scanning Confocal Acoustic Diagnostic Attenuation vs. Single BUA in $\text{cm}^2/\text{s}^2/\text{g}$



USA human bone measurement



Unique technology

- 1) Confocal ultrasonic technology to increase the spatial resolution and reduce noise.
- 2) Measuring both bone mineral density and bone strength.
- 3) Ultrasonic confocal point can be as fine as 0.1 mm, which is extremely useful.
- 4) 3-D scanning to identify bone quality in the region of interesting.
- 5) Fractal analysis of images determined by μ CT and ultrasound scanning, and determining their site-specific interrelationship and fractal coefficient.

Unique technology (cont.)

Determined bone quality coefficients

Bone Mineral Density index F_{BMD} :

$$F_{BMD}(\xi, \eta, \zeta) = P(\xi, \eta, \zeta) \Lambda(\xi, \eta, \zeta).$$

Where Λ is the coefficient parameter bridging the relation between ultrasound attenuation and BMD. ξ, η, ζ are the microstructural parameter determined by μ CT in porosity, BMC and trabecular width, respectively.

Bone strength index G_i :

$$G_i(\phi, \gamma, \tau) = \Gamma(\phi, \gamma, \tau) \rho V_i^2 \quad i = 1, 2, 3.$$

Where Γ is the coefficient parameter bridging the relation between ultrasound velocity and bone strength. ϕ, γ, τ are the microstructural parameter determined by μ CT. ρ is bone density; V is the ultrasonic velocity in three orthogonal directions.

Bone quality index H :

$$H(\mu, \gamma, \tau) = P(\mu, \gamma, \tau) \Lambda(\mu, \gamma, \tau) + \Gamma(\mu, \gamma, \tau) \rho V^2$$

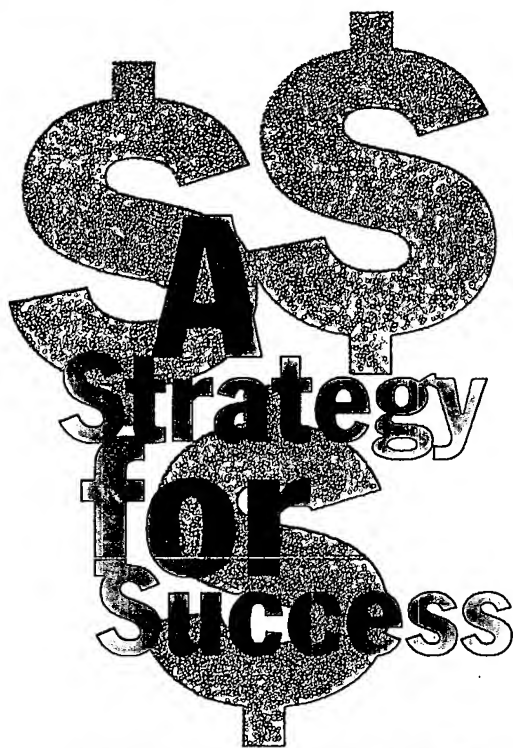
Where μ, γ, τ are the coefficients associated with μ CT and mechanical testing.

VENI, VIDI, INVENTI

A publication of the Center for Biotechnology

October/November, 2000

A New York State Center for Advanced Technology



Innovative Technology Development Program GOOD SCIENCE MAKES GOOD BUSINESS

Translating "good science into good business"... The Center for Biotechnology has been largely successful in fueling economic development in New York State by capitalizing on the tremendous resources inherent in the State's academic institutions. The Center's annual economic impact for fiscal year 1999-2000 alone is estimated at \$158M with 148 new jobs created.

A portion of the Center's success can be attributed to its unique Technology Development Initiative. The goals of the Initiative are to increase the number of income-producing technologies resulting from New York's research enterprise, while enhancing the financial value and return from these technologies by providing guidance and direct support in development toward commercial goals. The Initiative also aims to bundle synergistic technologies together to maximize value and to capture the economic benefit for New York State through the establishment of new companies and by out-licensing these "value-added" technologies to New York's bioscience industry.

The Center has begun to implement a winning formula for harnessing the enormous intellectual potential of New York State's academic institutions. A key component of

the Technology Development Initiative is the Innovative Technology Development (ITD) program which funds innovative, commercially promising, faculty research, alone or in partnership with industry. "No mechanism currently exists to adequately bridge the gap between discovery and early stage commercial development. As a result, a university's principal asset, its research, is often left undeveloped, its full commercial potential unrealized," states Clint Rubin, Director, Center for Biotechnology.

The ITD program aims to add value to technologies that will facilitate licensing, strategic partnerships, and/or new company formation. The Center fosters collaborative research and develops relationships with the biomedical industry as a means of accelerating discovery and development of technologies, and promoting faculty involvement with the bioscience industry sectors of New York State.

Through the ITD Program (formerly called the Innovative Technology Grant), the Center proactively identifies commercially promising technologies in New York State's academic institutions and systematically develops them for entry into the market. Unlike traditional models of technology transfer, research projects with commercial potential are nurtured by staff at the Center and developed beyond the initial concept stage. Corporate partners who license these technologies benefit from the reduced risk associated with the development of these more advanced technologies and from the accelerated product development cycle.

"Investment in basic research and the evolution of the biotechnology industry are inextricably linked. An investment in the discovery and development of commercially promising technologies within the academic environment will greatly increase the pool of income-producing technologies, yield greater returns, and generate new company formation," states Diane Fabel, Deputy Director, Center for Biotechnology.

Through the ITD program, the Center's Technology Development Initiative has already produced significant results. Four current-year ITD projects and two previously funded projects are under consideration for company formation. Two additional projects were co-sponsored by New York companies under the ITD program during the 1999/2000 fiscal year. In a collaboration between Roswell Park Cancer Institute and ZeptoMetrix (Buffalo, NY), DNA damage kits have been developed for research markets that have the potential to generate millions of dollars in revenue over the next five years. Vitex (Melville, NY), and SUNY Stony Brook are collaborating on the development of fibrin composites for treatment of severe wounds.

continued on page 2



The ITD program supports commercially promising research in all areas of medical biotechnology, including research products, diagnostics, medical devices, drug design, drug discovery, drug delivery, biomaterials, and bioengineering. Faculty at New York State research institutions, alone or in partnership with a New York State company, are eligible to apply. Applications in the area of diagnosis or treatment of chronic disease and hereditary disorders, cardiovascular disease, inflammation, infectious disease, cancer or cancer metastases, and research products with broad commercial potential are especially encouraged in this solicitation.

Objectives of the Program:

- Undertake high quality translational research with significant potential for economic payoff.
- Stimulate technological innovation and new product development through university/industry collaborations.
- Increase commercialization of university innovations through strategic industry partnerships or new company formation.
- Maximize economic benefit to New York State.
- Increase the value of intellectual property.

The Center will give preference to projects which hold strong potential for commercialization within the near term (2-5 years) in New York State.

Application Procedure:

Faculty considering submission of a proposal are encouraged to contact Dr. Anil Dhundale, Director for Scientific Affairs (anil.dhundale@sunysb.edu).

Application forms can be downloaded from the Center's web site at www.biotech.sunysb.edu or by calling the Center at 631-632-8521.

The deadline for all submitted written proposals is 5 p.m. Late proposals will not be considered.

Blumberg No. 5192

EXHIBIT

B

A Strategy for Success (continued from page 1)

Projects supported in previous years are also beginning to fulfill their commercial potential as well. 3D Virtual Colonoscopy, a technology supported by the Center in 1996-1998, has led to the formation of Viatronix (Stony Brook, NY), a company that will commercially exploit the medical applications of this imaging technology. Utilizing MRI and CAT scan data to create an image of a patient's colon, the technology allows doctors to non-invasively search for suspicious lesions. Functional Genetic Assay for Nuclear Import and Export, a research project supported by the Center (1997-2000), has resulted in a technology whose value has been greatly enhanced through the efforts of the Center's technology development staff. The technology is now available for license on a non-exclusive basis.

At least three Center-supported technologies are currently in human

clinical trials; a technology for the treatment of Dupuytren's Disease in partnership with Biospecifics Technologies Corp., (Lynbrook, NY); a technology for the early detection of cataracts; and a technology that uses polio recombinants as therapy for brain tumors.

Academic institutions will continue to play a significant role in the economic development of New York State. With the enactment of the J2K legislation, there is a recognition of the importance of strengthening the State's research infrastructure with the aim of fueling economic development in New York State. With this in mind, the Center will continue to develop its Technology Development Initiative to further bridge the intellectual wealth of New York State's academic institutions to the bioscience industry.

UNIQUE DIAGNOSTIC TOOL FOR USE IN OSTEOPOROSIS RESEARCH

**Center funds SUNY Stony Brook project
that uses ultrasound to detect bone quality**

Dr. Yi-Xian Qin, from the Program in Biomedical Engineering at Stony Brook University, is working on a project entitled, "A Scanning Confocal Acoustic Diagnostic (SCAD) for Bone Quality." This project is focused on developing a system that will be capable of detecting bone mass and quality using ultrasonic attenuation and velocity scanning. Techniques that utilize ultrasound provide an intriguing method for characterizing the material properties of bone in a manner that is non-invasive, non-destructive, and relatively accurate. Dr. Qin states, "The primary advantage of ultrasound, as applied with this technology, is that it allows for the measurement of not only bone density, but also bone quality."

SCAD will offer clinicians a diagnostic tool to determine the bone quality of patients suffering from various musculo-skeletal disorders, such as osteoporosis. Osteoporosis is a disease characterized by low bone mass and structural deterioration of bone tissue, leading to bone fragility and an increased susceptibility to fractures of the hip, spine, and wrist. According to the National Osteoporosis Foundation, 25 million Americans are currently afflicted with osteoporosis and 18 million are at risk because of low bone density. Studies estimate that as many as 1.5 million fractures occur each year due to an osteoporosis condition. This data becomes even more significant after considering the U.S. Census Bureau study "Data Base News in Aging" because the report indicates that the current elderly population (ages 55-85+) amounts to 21.5 million. Moreover, the baby boom generation, which includes only those between 35-55 years, amounts to an astounding 39 million people. Based on these data, the current trends of age-related health risks, such as osteoporosis, will increase dramatically throughout the next century.

Several potential commercialization strategies can be derived from Dr. Qin's technology, including licensing the intellectual property to an existing firm that may be interested in further development, or through the formation of a start-up corporation aimed at capitalizing on the market potential and competitive advantages of the technology. The Center is working closely with Dr. Qin and the Office of Technology Licensing to determine an appropriate development path. Dr. Qin states, "We are very excited about the commercialization opportunities, and the Center has been very helpful in moving this technology forward."

Companies interested in learning more about the potential of this technology should contact Rob Shorr, Director, Business Development, at the Center for Biotechnology at 631-632-8521.

INDUSTRY PARTNERSHIPS

TECHNOLOGY

CORPORATE PARTNER

Antisense Technology

Enzo Biochem

Intervenes at the genetic level making it theoretically possible to address any disease caused by the malfunction of a gene.

Antibody to Prevent Platelet Aggregation and Restenosis of Coronary Arteries

Centecor/Eli Lilly

Inhibits fibrinogen attachment thereby preventing platelet aggregation.

Modified Tetracycline Technology

Collagenex

Inhibits destruction of collagen with applications in the treatment of periodontal disease, cancer, osteoporosis, and osteoarthritis.

Biomaterial Applications of Hyaluronic Acid

Clear Solutions Biotech

HA has been chemically modified to produce novel biomaterials for drug-delivery and tissue engineering.

Genetic System to Detect Protein-Protein Interaction

45+ companies worldwide

Identifies the gene for an interactive protein of interest.

Improved Diagnosis of Lyme Borreliosis

Brook Biotechnology

Provides a major breakthrough in the sensitivity and accuracy in the diagnosis of Lyme disease.

Rapid Diagnostic Assay for Detecting Helicobacter pylori

Enteric Products

A system for detecting the presence of *H. pylori* in gastric juice by measuring ammonia concentration.

Low level Biomedical Prophylaxis for the Inhibition of Osteopenia

Exogen

Use of extremely low strain magnitudes at relatively high frequencies, to reverse the bone loss in aging.

3D Virtual Colonoscopy

Viatronix

A non-invasive cancer screening device that helps clinicians identify suspicious lesions.

VIATRONIX REVOLUTIONIZES DIAGNOSIS OF COLORECTAL CANCER USING "3D VIRTUAL COLONOSCOPY" TECHNOLOGY

Dr. Arië Kaufman, Leading Professor in Computer Science at the State University of New York (SUNY) at Stony Brook has developed a specialized computer software system for visualizing and interactively manipulating volumetric objects.

This project, which was supported by the Center for Biotechnology's innovative technology development program from 1991, has led to the development of a revolutionary 3D imaging technology called "3D Virtual Colonoscopy." The technology has the potential to replace invasive colonoscopy as a screening tool for colorectal cancer.

Viatrix, Inc., located in the Long Island High Technology Park at the SUNY Stony Brook campus, was specifically created to commercialize this technology. The technology

polyps. According to Viatrix, it is a revolutionary, non-invasive and highly improved tool for performing diagnostics in the area of colorectal cancer and allows for accurate spotting of pre-cancerous polyps before they become dangerous.

In 1999, an estimated 56,600 deaths occurred from patients with colorectal cancer, which makes it the second leading cause of cancer deaths in the U.S. However, with timely and accurate screening of the colon, and subsequent removal of polyps of a certain type and size, colorectal cancer can be prevented. Early screening is invaluable, as studies have shown that it may take up to 10 years for a polyp to grow large enough in size to result in the development of invasive and potentially deadly cancer. The incidence of colorectal cancer increases with age. The older the age of 50, the higher the risk of developing colorectal cancer. With colorectal cancer, the death rate is high, but it is not inevitable. When considering that this disease is the third leading cause of death in the U.S., the potential for early detection is significant.

Viatrix hopes to use this technology to provide clinicians with a virtually non-invasive diagnostic tool and to help in early detection of colorectal cancer. Regulatory applications have been submitted to the FDA in the form of a pre-clinical study. The technology is also being marketed by Viatrix, Inc. to the medical community. Viatrix, Inc. is a subsidiary of Viatrix, Inc., a company that has been established to commercialize this technology. Viatrix, Inc. is a subsidiary of Viatrix, Inc., a company that has been established to commercialize this technology.

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ALTERNATIVE CAREERS IN THE BIOSCIENCE INDUSTRY SEMINAR SERIES

The Center for Biotechnology, in partnership with the Career Center at SUNY Stony Brook, will be hosting a 7-part seminar series exploring the diverse career opportunities in the bioscience industry. This series is aimed at seniors and graduate students in the bioscience, engineering and life sciences with the goal of introducing students to the diverse and exciting career opportunities available in the bioscience industry. Key industry representatives from various sectors of the bioscience industry will present an insider look at their own personal career and provide background on their roles, responsibilities and career growth potential in their area of specialization.

"As academic opportunities dwindle, students are becoming increasingly frustrated with what to do with their educations," states Diane Fabel, Deputy Director, Center for Biotechnology. "The bioscience industry is growing exponentially and there is a need to increase the awareness among students of life on the corporate side," adds Ms Fabel.

Topics include alternative careers in law, corporate R & D, regulatory affairs, production, sales and technical support, entrepreneurship, and business development. Speakers scheduled include: Dr. Charles Ryan, J.D., Ph.D., Vice President, Technology Management and General Counsel, The Collaborative Group, Ltd. Stony Brook, New York; Daniel Yarosh, Ph.D., President and Chairman, AGI Dermatics; Philip N. Sussman, Executive Vice President of Corporate Development at Memory Pharmaceuticals Corp.; and Lillian Markind Bloch, Application Specialist, Affymetrix.

"Educating students as to industry needs is one of the key areas in the overall strategy of effective recruitment. This is a rare opportunity for students to engage in a productive dialogue with industry leaders about realistic career goals, aspirations and their future after graduation," states Angeline Judex, Communications Specialist, Center for Biotechnology. "The Center for Biotechnology is aggressively pursuing a mandate of bridging the 'awareness' gap between students and the bioscience industry. We want students to know of the many exciting opportunities now available in the industry upon graduation."

This seminar series is one of the workforce development initiatives put in place by the Center. The Center for Biotechnology also runs the Undergraduate Research Internship program and the Graduate Internship program in Biotechnology and Patent Law.

The seminar series will be held on the SUNY Stony Brook campus. More information on the series can be found at www.biotech.sunysb.edu

This series is organized by the Center for Biotechnology and the Career Center at SUNY Stony Brook, and presented on behalf of the Long Island Life Sciences Initiative.

Wednesday, Sep 27, 5pm CAT
"From the Bench to the Bar"
Alternative Careers in Law
Dr. Charles Ryan,
VP Technology Development
and General Counsel
Collaborative Group, Long Island, NY

Tuesday, Oct 24, 5pm LS 038*
"Converting Science into Products"
Careers in Corporate R & D
Dr. Anil Dhundale,
Director Scientific Affairs
Center for Biotechnology

Tuesday, Nov. 28, 5pm LS 038*
"\$High Risk, High Return\$"
Careers in the World of Finance
Dr. Robert Shorr,
Director, Business Development
Center for Biotechnology

Tuesday, Feb 27, LS 038*
"A Dollar and a Dream"
Life as an Entrepreneur
Daniel Yarosh, Ph.D.
President and Chairman
AGI Dermatics

Tuesday, Mar 27, LS 038*
**"The Strategy Beyond
the Science"**
**Careers in Business
Development**
Philip N. Sussman,
Executive Vice President
of Corporate Development,
Memory Pharmaceuticals Corp., NY

Tuesday, Apr 24, LS 038*
**"\$400M and a Decade Later,
It's Time to Produce the Goods"**
**Careers in Regulatory Affairs;
Clinical Trial Management,
and cGMP Production**
Dr. Jules T. Mitchel, Ph.D.
President
Target Health Inc., NY

Tuesday, May 15, LS 038*
"Making it Happen"
**Careers in Technical Support,
Sales and Marketing**
Lillian Markind Bloch
Application Specialist
Affymetrix

Bioengineering and Biotechnology Seminar Series, 2000-2001

4:00pm on Wednesday Afternoons, Atkins Learning Center, 4th Floor, Health Sciences Center SUNY Stony Brook

September 13, 2000
Organization of Bone and Other Mineralized Tissues:
Insight into Mechanism of Biological Mineralization
Melvin Glimcher, M.D.
Harriet M. Peabody Professor of Orthopaedic Surgery
Harvard Medical School, Boston, MA

October 18, 2000
cDNA Microarrays; The Opportunities and
Challenges of a New Genomics Technology
Anil Dhundale, Ph.D.
Director of Scientific Affairs, Center for Biotechnology
State University of New York at Stony Brook

November 15, 2000
From Benchtop to Bedside; The Travails of
Bringing Bone Morphogenic Protein to the Clinic
Howard Seeherman, Ph.D., V.M.D.
Senior Scientist
Genetics Institute, Cambridge, MA

December 13, 2000
The Early Response in Functional MRI
Thomas Ernst, Ph.D.
Director of Medical Physics
Brookhaven National Laboratory, Upton, NY

February 14, 2001
Tissue Engineering of the Musculoskeletal System
Rocky S. Tuan, Ph.D.
Professor of Orthopaedic Surgery, Biochemistry
& Molecular Pharmacology
Thomas Jefferson University, Philadelphia, PA

March 14, 2001
Engineering of Cardiovascular Tissues
Robert M. Nerem, Ph.D.
Professor and Director
Parker H. Petit Institute for Bioengineering and Bioscience
Georgia Institute of Technology

April 11, 2001
High Speed Genomic Sequencing: A Unique
Approach to Improved Sensitivity
Vera Gorfinkel, Ph.D.
Associate Professor of Electrical Engineering
State University of New York at Stony Brook

May 9, 2001
Molecular Mechanisms of Fracture Healing:
Can Intervention Improve on Mother Nature?
Mark Bolander, M.D.
Professor of Orthopaedic Surgery, Mayo Clinic, Rochester, MN

For further information, please contact: The Program in Biomedical Engineering at 631-632-2302

Veni, Vidi, Inveni, a publication of the Center of Biotechnology, is published quarterly. We welcome comments, suggestions and submissions.

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